

REMARKS

A. Background

By this paper, claims 1–2, and 4-18 are amended, and claim 3 is cancelled. Accordingly, claims 1–2 and 4-18 are currently pending. Applicants respectfully request entry of the amendments herein prior to examination of the application and favorable consideration of the pending claims.

B. Objections to Specification

The Office Action has objected to the specification for various reasons. In response, the Applicant hereby has amended the specification to correct the errors identified in the Office Action.

A section of "Brief Description of the Figures" and accompanying paragraphs have been added into the specification to provide the brief description of the figures.

Paragraphs 1, 10, 12, 14, and 16 have been amended to recite "pharmaceutically combined preparation" as requested in the Office Action.

Paragraph 4 has been amended to recite "Human serum albumin (HSA)" as requested in the Office Action.

Paragraph 9 has been amended to recite "sulfhydryl groups (SH-groups)" as requested in the Office Action.

Paragraph 10 has been amended to recite "10,000" instead of "10.000" as requested in the Office Action. Such a change does not constitute new matter because one of ordinary skill in the art knows that some countries use commas and others use periods when reciting such numbers. However, the "thiol groups" is not incorrect, and withdrawal of this rejection is respectfully requested.

Paragraph 13 has been amended to recite "glutathione (GSH)" as requested in the Office Action.

Paragraph 32 has been amended to recite "NO₂⁻- and NO-radical" which was partially requested in the Office Action. Note that "NO₂⁻-" is correct in the context that the hyphen is correct with regard to the hyphen in front of radical (e.g., "-radical"). Also, the "NO-radical" is correct and the "dash" is a hyphen and not a minus sign, and thereby the "dash" does not need to be a superscript.

Paragraph 57 has been amended to recite "the NO-group is cleaved selectively from an S-nitrosated compound (RS—NO; where R represents a compound having the S-nitrosated group) by Hg^{2+} ". This amendment does not introduce any new matter because one of skill in the art would understand that the "R" in the "RS-NO" is an indication that "R" is any group, such as a protein as described herein, and "R" is a common representation in chemistry that the entity represented by "R" can vary. The amended language merely clarifies what "R" is.

Paragraph 63 has been amended to recite "(tidal volume=0.0062x body weight (kg)^{1.01}, respiration rate=53.5x body weight (kg)^{-0.26}).". Such a change does not constitute new matter because one of ordinary skill in the art knows that some countries use commas and others use periods when reciting such numbers.

In view of the foregoing amendments to the specification, Applicant respectfully request withdrawal of the objections to the specification.

C. Objections to Claims

The Office Action has objected to claims 1-18 for various reasons. In response, the Applicant hereby has amended the claims to correct the errors identified in the Office Action.

Claim 1 has been amended so that the claim does not recite non-elected subject matter.

Claim 3 has been cancelled.

Claim 4 is correct because there was only an election of species for the "compound containing thiol groups" and claim 4 recites "reduced glutathione" which was elected by the Applicant. Withdrawal of this objection is respectfully requested.

Claims 6, 14, and 14-18 are correct because the compounds being recited are for the "compound containing thiol groups" which was only subject to an election of species and "reduced glutathione" is recited. Withdrawal of this objection is respectfully requested.

D. Objections to Drawings

The Office Action objected to the drawings of Figures 1c, 2a, 2b, 3a, 3b, and 4a-4b. In response, Replacement Sheets are being filed herewith to correct the drawings.

E. Claim Rejections Under § 101

The Office Action rejected claims 1-18 under 35 U.S.C. § 101. In response, Applicant has amended claims 1-18 to recite that the claims are for a "method of treatment" as elected in response to the Restriction Requirement. Withdrawal of this rejection is respectfully requested.

F. Claim Rejections Under § 112

The Office Action rejected claims 1-18 under 35 U.S.C. § 112, second paragraph.

Applicant believes that claim 1 as amended herein clarifies the language so that it is now clear that it is the "compound containing thiol groups" that has "an average molecular weight of at most 10,000." Also, claim 1 has been amended to recite method steps.

Claim 2 has been amended to clarify that it is the SH-groups of the therapeutic protein that are being described.

Claim 3 has been cancelled.

Claim 4 has been amended for clarification.

Claims 7 and 14-18 have been amended for clarification.

Applicant respectfully asserts that claims 8 and 9 each has sufficient antecedent basis because there is no requirement to affirmatively recite the "S-nitroso albumin" or "reduced glutathione" as in claims 8 and 9. The terminology as written in claims 1, 2, 8, and 9 provide a sufficient antecedent basis for these terms. The antecedent for "S-nitroso albumin" in claim 8 is "a therapeutic protein S-nitroso albumin having SH-groups which are nitrosated" as recited in claim 1. The antecedent for "reduced glutathione" in claim 9 is "a compound containing thiol groups and having an average molecular weight of at most 10,000," as recited in claim 1.

Applicant respectfully asserts that claims 10-12 as written are not in violation of the antecedent basis requirement for the terms "S-nitroso albumin" or "reduced glutathione." Claim 1 provides sufficient antecedent basis for the terminology.

In view of the foregoing, Applicant respectfully requests withdrawal of this rejection because all of the claims comply with the §112, second paragraph requirement.

G. Claim Rejections Under § 103

The Office Action rejected claims 1-18 under 35 U.S.C. § 103(a) as being unpatentable over Schlag et al (US 6,358,918) in view of Tsikas et al (*Biochem. Biophys. Acta* (2001) 1546, 422-434) and Hallstrom et al (Hallstrom et al (2002) *Circulation*, 105, 3032-3038). Applicant respectfully traverses because a *prima facie* case of obviousness has not been established.

In accordance with Applicant's understanding, Schlag discloses a method of treating cerebral ischemia in a patient by administering a pharmaceutical composition having thiol-group-containing proteins that are nitrosated. On the other hand, Schlag does not teach or suggest that ischemia can be treated with a pharmaceutical composition having "a compound containing thiol groups and having an average molecular weight of at most 10,000."

Additionally, Schlag does not teach or suggest that ischemia can be treated with a pharmaceutical preparation having a combination of a protein with SH groups being nitrosated in combination with a compound containing thiol groups with an average molecular weight of not more than 10,000. As such, Schlag does not teach or suggest each and every element of the currently pending claims.

According to Applicant's understanding, Tsikas teaches transnitrosylation of albumin in vivo and in vitro. Tsikas assumes that it is likely that S-transnitrosilation of albumin in vivo is done by S-nitrosocysteine or S-nitrosogluthathione rather than by NO itself. Tsikas is completely silent with respect to the treatment of ischemia. Tsikas is also silent about a combined preparation of S-nitroso albumin with a compound containing thiol groups with an average molecular weight of not more than 10,000. Therefore, Tsikas does not teach or suggest each and every element of the currently pending claims.

In accordance with Applicant's understanding, Hallstrom discloses that S-nitroso human serum albumin treatment reduces ischemia injury in skeletal muscle via NO release. Hallstrom also investigates mechanisms that reduce the total amount of NO and proposes a treatment with S-nitroso human serum albumin. Hallstrom is silent about a combination of S-nitroso albumin with a compound containing thiol groups with an average molecular weight of not more than 10,000. Hallstrom does not suggest any combined preparation of S-nitroso human serum albumin with another compound.

In view of the foregoing, Applicant respectfully asserts that the combination of references does not teach or suggest each and every element of the presently pending claims. Specifically, the combination of references does not teach or suggest "administering to a subject a pharmaceutical preparation having a therapeutic protein S-nitroso albumin having SH-groups which are nitrosated, and a compound containing thiol groups and having an average molecular weight of at most 10,000 for treating ischemia," as recited in claim 1. While each of Schlag, Tsikas and Hallstom teach proteins having nitrosated thiol groups, none of these references teach combining the proteins having nitrosated thiol groups with a compound containing thiol groups and having an average molecular weight of at most 10,000 for treating ischemia. In fact, Tsikas is silent with regard to treating ischemia. An each reference in the combination is silent with regard to a compound containing thiol groups and having an average molecular weight of at most 10,000 for treating ischemia. Accordingly, even when combined the combination of references

do not teach or suggest a pharmaceutical preparation for treating ischemia that includes "a therapeutic protein S-nitroso albumin having SH-groups which are nitrosated, and a compound containing thiol groups and having an average molecular weight of at most 10,000." Thus, the combination of references does not teach or suggest each and every element of the currently pending claim 1.

Applicant respectfully asserts that the combination of Schlag, Tsikas, and Hallstrom teach away from the presently claimed invention because Schlag teaches away from low molecular weight proteins that are under 10,000 molecular weight. Schlag recites "[A]ccording to the present invention, high-molecular proteins are preferred over low-molecular proteins, such as, e.g., glutathione." (col. 2, lines 60 to 62). Accordingly, Schlag teaches away from using a compound that contains thiol groups with an average molecular weight of not more than 10,000, and thereby teaches away from using reduced glutathione. Neither Tsikas nor Hallstrom correct this "teaching away," and thereby the combination of references teaches away from the presently claimed invention recited in claim 1.

Since the combination of references does not teach or suggest each and every element of the currently pending claim 1 and Schlag actually teaches away from the currently pending claim 1, a *prima facie* case of obviousness has not been established. Claim 1 is thereby allowable, and because claims 2, and 4-18 depend from claim 1, claims 2, and 4-18 are allowable for the same reasons claim 1 is allowable. Applicant respectfully requests withdrawal of this rejection under 35 U.S.C. § 103(a).

H. CONCLUSION

In view of the foregoing, Applicant respectfully submits that the other rejections to the claims are now moot and do not, therefore, need to be addressed individually at this time. It will be appreciated, however, that this should not be construed as Applicant acquiescing to any of the purported teachings or assertions made in the last action regarding the cited art or the pending application, including any official notice. Instead, Applicant reserves the right to challenge any of the purported teachings or assertions made in the last action at any appropriate time in the future, should the need arise. Furthermore, to the extent that the Examiner has relied on any Official Notice, explicitly or implicitly, Applicant specifically requests that the Examiner

provide references supporting the teachings officially noticed, as well as provide the required motivation or suggestion to combine references with the other art of record.

For at least the foregoing reasons, Applicant respectfully submits that the pending claims are neither anticipated by nor made obvious by the art of record. In the event that the Examiner finds any remaining impediment to a prompt allowance of this application that may be clarified through a telephone interview, the Examiner is requested to contact the undersigned attorney.

Dated this 16th day of March 2010.

Respectfully submitted,

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